

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**In re the Application of: ITO, et al****Confirmation No. 2230****Serial No.: 10/539,188****Group Art Unit: 1621****Filed: June 16, 2005****Examiner: Chukwuma O Nwanichu****FOR: METHOD FOR DEUTERATION****DECLARATION****Commissioner of Patents and Trademarks****Washington, DC 20231****Sir:**

I, Nobuhiro ITO, a Japanese citizen, residing at 1-16-21 Shimachi, Tsurugashima, Saitama, Japan do hereby solemnly and sincerely declare and state:

THAT I am by profession a research chemist having been awarded a master's degree from the graduate course of the Synthetic chemistry at Gifu Pharmaceutical University, in March, 1996;

THAT I began employment with Wako Pure Chemical Industries, Ltd., the Assignee of the above-identified application, in April, 1996 and have been engaged, since that time, in research and study of process chemistry in the Tokyo Research Laboratories;

THAT I received Ph. D. from Gifu Pharmaceutical University, in December, 2008;

THAT I am a co-inventor of the invention disclosed in the above-identified U.S. patent application and am well aware of the prosecution history thereof;

THAT, I conducted the following Experiment with my best knowledge honestly and sincerely.

EXPERIMENT

1. Comparative Example

The same deuteration reaction was conducted under the same conditions as those used in Example 4 of the present application, except that NaOH was added. The detailed method was as follows.

In 17 mL of deuterium oxide (D_2O) was suspended 500mg of 2-heptanone (substrate, 4.38 mmol), 50 mg of 10% palladium carbon and 350 mg of NaOH (8.76 mmol), followed by replacing the atmosphere of a sealed reaction system with hydrogen gas (H_2) and conducting a reaction in an oil bath at 160°C for 24 hours. After completion of the reaction, the reaction solution was diluted with Et_2O (20 mL), followed by filtering off the catalyst from the reaction mixture. Then, the filtrate was neutralized by adding dilute hydrochloric acid solution, and a gel-like product was obtained.

2. Result

As it is clear from the result of the above comparative example, it is understood that a reaction of a substance using D_2O in the presence of an activated catalyst (a catalyst and H_2) under basic condition (NaOH) results in decomposition of the substance and formation of a gel-like product.

Therefore, it is found that a deuteration reaction under basic condition cannot efficiently deuterate a substrate that is liable to decomposition under basic condition such as a ketone.

I, the undersigned declarant, declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and; further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signed this 31st day of March, 2009.

Nobuhiko Ito

Nobuhiko ITO